

EXAMINER'S NOTES

Access DB:

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Reluina Cook Examiner #: 69824 Date: 1/52886
Art Unit: 1614 Phone Number: 301-157-1170 Serial Number: 101602303
Mail Box and Bldg/Room Location: 3070 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please provide structures of compounds & claim to search them + curcumin to treat multiple myeloma.

Search inventor's own work.

Search in Cancerlit, Medline & other DB's as appropriate

Appropriate

Thank you
Reluina

=> d his ful

FILE 'REGISTRY' ENTERED AT 10:42:10 ON 16 MAY 2005

L1 7 SEA ABB=ON (VINCRISTINE OR BCNU OR MELPHALAN OR CYCLOPHOSPHAMI
DE OR ADRIAMYCIN OR PREDNISONE OR DEXAMETHASONE)/CN
L2 1 SEA ABB=ON CURCUMIN/CN

FILE 'HCAPLUS' ENTERED AT 11:01:38 ON 16 MAY 2005

L3 83 SEA ABB=ON (L1 OR VINCRISTINE OR BCNU OR MELPHALAN OR
CYCLOPHOSPHAMIDE OR ADRIAMYCIN OR PREDNISONE OR DEXAMETHASONE)
AND (L2 OR ?CURCUMIN?)
L4 7 SEA ABB=ON L3 AND ?MULTIPLE? (W) ?MYELOMA? *7 cit's from CAPLUS*
D AU 1-7

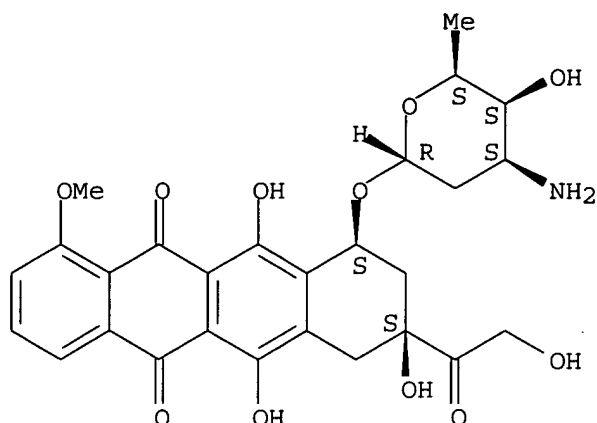
FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
11:03:05 ON 16 MAY 2005

L5 14 SEA ABB=ON L4
L6 8 DUP REMOV L5 (6 DUPLICATES REMOVED) *8 cit's from other d.b.s*

=> d 11

L1 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
RN 25316-40-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy- α -L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, hydrochloride, (8S,10S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy- α -L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, hydrochloride, (8S-cis)-
CN Adriamycin, hydrochloride (8CI)
OTHER NAMES:
CN ADM hydrochloride
CN ADR
CN Adriablastina CS
CN Adriacin
CN **Adriamycin**
CN Adriblastin
CN Adriblastina
CN Adriblastina RD
CN DOX HCl
CN Doxorubicin hydrochloride
CN FI 106
CN FI 6804
CN Hydroxydaunorubicin hydrochloride
CN Lipodox
FS STEREOSEARCH
MF C27 H29 N O11 . Cl H
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSChem, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDb, IMSPATENTS, IPA, MRCK*, MSDS-OHS, NIOSHTIC, PATDPASPC, PROMT, PROUSDDR, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (23214-92-8)

Absolute stereochemistry.



● HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4562 REFERENCES IN FILE CA (1907 TO DATE)

240 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

4571 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

L1 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 154-93-8 REGISTRY

ED Entered STN: 16 Nov 1984

CN Urea, N,N'-bis(2-chloroethyl)-N-nitroso- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Urea, 1,3-bis(2-chloroethyl)-1-nitroso- (8CI)

OTHER NAMES:

CN 1,3-Bis(β-chloroethyl)-1-nitroso-urea

CN 1,3-Bis(2-chloroethyl)-1-nitroso-urea

CN 1,3-Bis(2-chloroethyl)-1-nitroso-urea

CN **BCNU**

CN Becenun

CN BiCNU

CN Carmubris

CN Carmustin

CN Carmustine

CN DTI 015

CN FDA 0345

CN Gliadel

CN N,N'-Bis(2-chloroethyl)-N-nitroso-urea

CN Nitrumon

CN NSC 409962

CN SK 27702

CN SRI 1720

FS 3D CONCORD

MF C5 H9 Cl2 N3 O2

CI COM

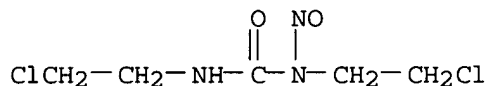
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT,

CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

2596 REFERENCES IN FILE CA (1907 TO DATE)

38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

2603 REFERENCES IN FILE CAPLUS (1907 TO DATE)

23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L1 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 148-82-3 REGISTRY

ED Entered STN: 16 Nov 1984

CN L-Phenylalanine, 4-[bis(2-chloroethyl)amino]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Alanine, 3-[p-[bis(2-chloroethyl)amino]phenyl]-, L- (8CI)

OTHER NAMES:

CN 3025CB

CN Alanine nitrogen mustard

CN Alkeran

CN CB 3025

CN L-PAM

CN L-Phenylalanine mustard

CN L-Phenylalanine mustard hydrochloride

CN L-Sarcolysin

CN L-Sarcolysine

CN L-Sarkolysin

CN Levofalan

CN Levofolan

CN Levopholan

CN Melfalan

CN **Melphalan**

CN NSC 241286

CN NSC 8806

CN Phenylalanine mustard

CN Sarcoclorin

FS STEREOSEARCH

DR 8057-25-8

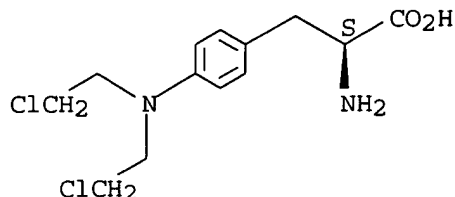
MF C13 H18 Cl2 N2 O2

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)
 Other Sources: EINECS**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3115 REFERENCES IN FILE CA (1907 TO DATE)
 173 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 3121 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 21 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L1 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 57-22-7 REGISTRY

ED Entered STN: 16 Nov 1984

CN Vincaleukoblastine, 22-oxo- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Indolizino[8,1-cd]carbazole, vincaleukoblastine deriv.

CN 2H-3,7-Methanoazacycloundecino[5,4-b]indole, vincaleukoblastine deriv.

CN Leurocristine (7CI, 8CI)

OTHER NAMES:

CN (+)-Vincristine

CN 22-Oxovincaleukoblastine

CN LCR

CN Leucristine

CN OncoTCS

CN VCR

CN Vincristin

CN **Vincristine**

CN Vinkristin

FS STEREOSEARCH

DR 28379-27-3

MF C46 H56 N4 O10

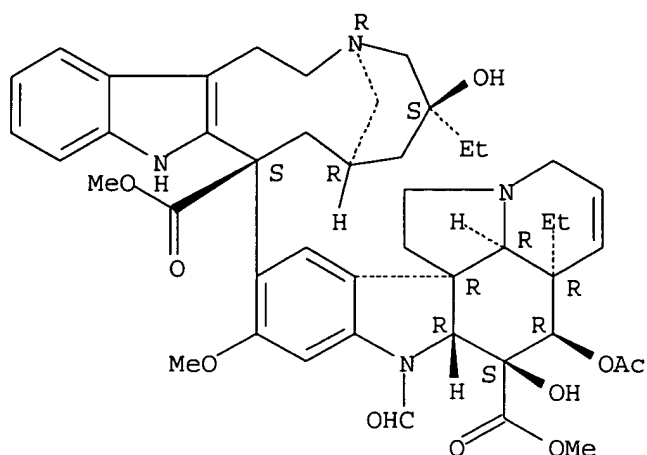
CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMLIST, CIN, CSCHM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PROMT, PROUSDDR, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
 (*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5937 REFERENCES IN FILE CA (1907 TO DATE)
122 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5948 REFERENCES IN FILE CAPLUS (1907 TO DATE)
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L1 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 53-03-2 REGISTRY

ED Entered STN: 16 Nov 1984

CN	Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy- (8CI, 9CI) (CA INDEX NAME)
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OTHER NAMES:

CN	Δ -Cortisone
CN	Δ^1 -Cortisone
CN	Δ^1 -Dehydrocortisone
CN	1,2-Dehydrocortisone
CN	1,4-Pregnadiene-17 α ,21-diol-3,11,20-trione
CN	1-Dehydrocortisone
CN	17,21-Dihydroxypregn-1,4-diene-3,11,20-trione
CN	17,21-Dihydroxypregna-1,4-diene-3,11,20-trione
CN	17 α ,21-Dihydroxy-1,4-pregnadiene-3,11,20-trione
CN	Adasone
CN	Ancortone
CN	Apo-Prednisone
CN	Bicortone
CN	Cartancyl
CN	Colisone
CN	Cordrol
CN	Cortan
CN	Cortidelt
CN	Dacorten
CN	Dacortin
CN	Decortancyl
CN	Decortin
CN	Decortisyl
CN	Dehydrocortisone
CN	Dekortin

CN Delcortin
CN Dellacort
CN Dellacort A
CN Delta E
CN Delta-Cortelan
CN Delta-Dome
CN Deltacortene
CN Deltacortisone
CN Deltacortone
CN Deltasone
CN Deltison
CN Deltisona
CN Deltisone
CN Deltra
CN Di-Adreson
CN Drazone
CN Econosone
CN Encorton
CN Encortone
CN Enkorton
CN Fernisone
CN Hostacortin
CN Liquid Pred
CN Me-Korti
CN Metacortandracin
CN **Prednisone**

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
DISPLAY

FS STEREOSEARCH

DR 68-59-7

MF C21 H26 O5

CI COM

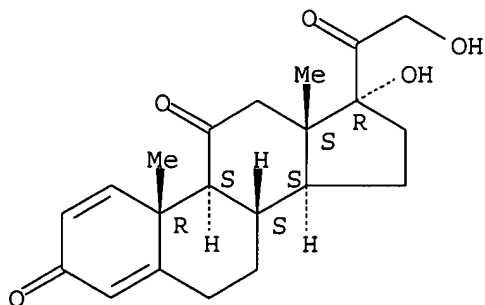
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,
CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*,
HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*,
MSDS-OHS, NIOSHTIC, PHAR, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER,
USAN, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: EINECS**, NDSL**, TSCA**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5047 REFERENCES IN FILE CA (1907 TO DATE)
54 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5056 REFERENCES IN FILE CAPLUS (1907 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L1 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 50-18-0 REGISTRY

ED Entered STN: 16 Nov 1984

CN 2H-1,3,2-Oxazaphosphorin-2-amine, N,N-bis(2-chloroethyl)tetrahydro-,
2-oxide (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2H-1,3,2-Oxazaphosphorine, 2-[bis(2-chloroethyl)amino]tetrahydro-, 2-oxide
(6CI, 8CI)

OTHER NAMES:

CN (+)-Cyclophosphamide

CN (RS)-Cyclophosphamide

CN 2-[Bis(2-chloroethyl)amino]tetrahydro-2H-1,3,2-oxazaphosphorin 2-oxide

CN Asta B 518

CN B 518

CN Bis(2-chloroethyl)phosphoramidate cyclic propanolamide ester

CN CB 4564

CN Clafen

CN Claphene

CN CP

CN CPA

CN CTX

CN CY

CN Cycloblastin

CN Cyclophosphamid

CN **Cyclophosphamide**

CN Cyclophosphamidum

CN Cyclophosphan

CN Cyclophosphane

CN Cyclostin

CN Cytophosphan

CN Cytoxan

CN Endoxan

CN Endoxan R

CN Endoxan-Asta

CN Endoxana

CN Endoxanal

CN Endoxane

CN Enduxan

CN Genoxal

CN Hexadrin

CN Mitoxan

CN N,N-Bis(β -chloroethyl)-N',O-trimethylenephosphoric acid ester diamide

CN N,N-Bis(2-chloroethyl)-N',O-propylenephosphoric acid ester diamide

CN NCI C04900

CN Neosar

CN Neosar (antineoplastic)

CN NSC 26271

CN Procytox

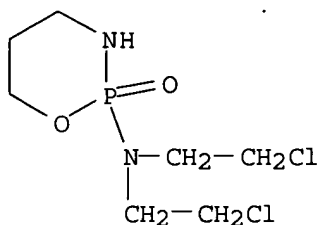
CN Semdoxan

CN Sendoxan

CN Senduxan

CN SK 20501

CN Zyklophosphamid
 FS 3D CONCORD
 DR 60007-95-6, 75526-90-8
 MF C7 H15 Cl2 N2 O2 P
 CI COM
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS,
 BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,
 CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSChem, CSNB, DDFU, DIOGENES,
 DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDb, IMSCoSEARCH, IPA, MEDLINE,
 MRCK*, MSDS-OHS, NIOSHTIC, PATDPASPC, PHAR, PROMT, PS, RTECS*, SPECINFO,
 TOxCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
 (*File contains numerically searchable property data)
 Other Sources: EINECS**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13479 REFERENCES IN FILE CA (1907 TO DATE)
 218 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 13505 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 256 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L1 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 50-02-2 REGISTRY

ED Entered STN: 16 Nov 1984

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-,
 (11 β ,16 α)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1-Dehydro-16 α -methyl-9 α -fluorohydrocortisone
 CN 16 α -Methyl-9 α -fluoro- Δ 1-hydrocortisone
 CN 16 α -Methyl-9 α -fluoro-1,4-pregnadiene-11 β ,17 α ,21-
 triol-3,20-dione
 CN 16 α -Methyl-9 α -fluoro-11 β ,17 α ,21-trihydroxypregna-
 1,4-diene-3,20-dione
 CN 16 α -Methyl-9 α -fluoroprednisolone
 CN 9-Fluoro-11 β ,17,21-trihydroxy-16 α -methylpregna-1,4-diene-3,20-
 dione
 CN 9 α -Fluoro-11 β ,17 α ,21-trihydroxy-16 α -methyl-1,4-
 pregnadiene-3,20-dione
 CN 9 α -Fluoro-16 α -methyl-1,4-pregnadiene-11 β ,17 α ,21-
 triol-3,20-dione
 CN 9 α -Fluoro-16 α -methyl-11 β ,17,21-trihydroxypregna-1,4-diene-
 3,20-dione
 CN 9 α -Fluoro-16 α -methylprednisolone
 CN Adexone
 CN Aeroseb-Dex

CN Aphtasolon
CN Aphthasolone
CN Azium
CN Calonat
CN Corsone
CN Cortisumman
CN Decacort
CN Decaderm
CN Decadron
CN Decadron A
CN Decalix
CN Decasone
CN Dekacort
CN Delipos
CN Deltafluorene
CN Dergramin
CN Deronil
CN Desadrene
CN Desameton
CN Deseronil
CN Dexa-Cortidelt
CN Dexa-Mamallet
CN Dexa-Scheroson
CN Dexa-sine
CN Dexacort
CN Dexacortal
CN Dexacortin
CN Dexadeltone
CN Dexafarma
CN Dexalona
CN Dexaltin
CN Dexameth
CN **Dexamethasone**
CN Dexamethasone alcohol
CN Dexamonozon
CN Dexapolcort
CN Dexapos
CN Dexaprol

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
DISPLAY

FS STEREOSEARCH

DR 8054-59-9, 137098-19-2

MF C22 H29 F O5

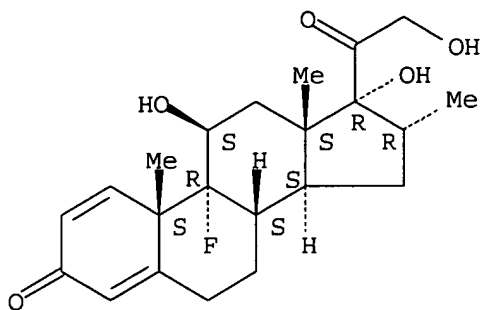
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS,
CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSChem, CSNB, DDFU,
DIOGENES, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDb,
IMSCoSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, PS,
RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)

Other Sources: EINECS**, NDSL**, TSCA**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

22723 REFERENCES IN FILE CA (1907 TO DATE)
 295 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 22759 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 186 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

=> d 12

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN

RN 458-37-7 REGISTRY

ED Entered STN: 16 Nov 1984

CN 1,6-Heptadiene-3,5-dione, 1,7-bis(4-hydroxy-3-methoxyphenyl)-, (1E,6E)-
 (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,6-Heptadiene-3,5-dione, 1,7-bis(4-hydroxy-3-methoxyphenyl)-, (E,E)-
 (8CI)

CN **Curcumin (6CI)**

OTHER NAMES:

CN (E,E)-1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione

CN C Yellow 15

CN C.I. 75300

CN C.I. Natural Yellow 3

CN Curcuma

CN Curcumin I

CN Curcumine

CN Diferuloylmethane

CN E 100

CN E 100 (dye)

CN Haidr

CN Halad

CN Haldar

CN Halud

CN Indian Saffron

CN Kacha Haldi

CN Merita Earth

CN Natural Yellow 3

CN NSC 32982

CN San-Ei Curcumine AL

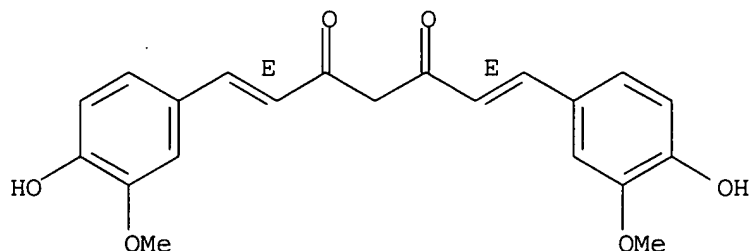
CN San-Ei Gen Curcumine AL

CN Souchet

CN Terra Merita

CN trans,trans-Curcumin
CN Turmeric
CN Turmeric (dye)
CN Turmeric yellow
CN Ukon
CN Ukon (dye)
CN Yellow Ginger
CN Yellow Root
CN Yo-Kin
FS STEREOSEARCH
DR 15845-47-3, 73729-23-4, 79257-48-0, 91884-86-5, 33171-04-9
MF C21 H20 O6
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS,
CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHM, DDFU, DIOGENES,
DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSRESEARCH, IPA,
MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT,
PROUSDDR, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USPAT2,
USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2080 REFERENCES IN FILE CA (1907 TO DATE)
110 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2091 REFERENCES IN FILE CAPLUS (1907 TO DATE)
21 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

=> d que stat 14

L1 7 SEA FILE=REGISTRY ABB=ON (VINCRISTINE OR BCNU OR MELPHALAN OR
CYCLOPHOSPHAMIDE OR ADRIAMYCIN OR PREDNISONE OR DEXAMETHASONE)/
CN

L2 1 SEA FILE=REGISTRY ABB=ON CURCUMIN/CN

L3 83 SEA FILE=HCAPLUS ABB=ON (L1 OR VINCRISTINE OR BCNU OR
MELPHALAN OR CYCLOPHOSPHAMIDE OR ADRIAMYCIN OR PREDNISONE OR
DEXAMETHASONE) AND (L2 OR ?CURCUMIN?)

L4 7 SEA FILE=HCAPLUS ABB=ON L3 AND ?MULTIPLE?(W)?MYELOMA?

L4 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:185396 HCAPLUS

DOCUMENT NUMBER: 142:254582

TITLE: **Curcuminoids** as selective inhibitors of
STAT-3 activation and uses in treating cancer or
precancer

INVENTOR(S): Aggarwal, Bharat B.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 31 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005049299	A1	20050303	US 2004-925814	20040825
WO 2005020908	A2	20050310	WO 2004-US27578	20040825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-497842P P 20030826

AB The present invention provides a method of treating a cancerous or
pre-cancerous state in an individual in need of such treatment, comprising
the step of administering a pharmacol. ED of a **curcuminoid** to
the individual. **Curcumin** inhibited interleukin 6-induced
proliferation of human **multiple myeloma** cells.

L4 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:533970 HCAPLUS

DOCUMENT NUMBER: 141:65088

TITLE: Methods and compositions for the prevention or
treatment of neoplasia comprising a COX-2 inhibitor in
combination with an epidermal growth factor receptor
antagonist

INVENTOR(S): Masferrer, Jaime

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S.

Ser. No. 470,951.

CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 21
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004127470	A1	20040701	US 2003-651916	20030829
EP 1522313	A1	20050413	EP 2004-26577	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO, CY				
WO 2005037259	A2	20050428	WO 2004-US27574	20040825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
 US 1998-113786P P 19981223
 US 1999-470951 B2 19991222
 US 1999-385214 A 19990827
 EP 1999-968939 A3 19991222
 US 2003-651916 A 20030829

AB The present invention relates to a novel method of preventing and/or treating neoplasia disorders in a subject that is in need of such prevention or treatment by administering to the subject at least one COX-2 inhibitor in combination with an EGF receptor antagonist. Compns., pharmaceutical compns. and kits are also described.

L4 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:342327 HCAPLUS

DOCUMENT NUMBER: 140:368302

TITLE: Nuclear factor- κ B and STAT3 are constitutively active in CD138+ cells derived from **multiple myeloma** patients, and suppression of these transcription factors leads to apoptosis

AUTHOR(S): Bharti, Alok C.; Shishodia, Shishir; Reuben, James M.; Weber, Donna; Alexanian, Raymond; Raj-Vadhan, Saroj; Estrov, Zeev; Talpaz, Moshe; Aggarwal, Bharat B.

CORPORATE SOURCE: Departments of Bioimmunotherapy, Hematopathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Blood (2004), 103(8), 3175-3184

CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chemoresistance is a major problem in the treatment of patients with **multiple myeloma** (MM). Because of the central role of the nuclear transcription factors nuclear factor- κ B (NF- κ B) and signal transducer and activator of transcription 3 (STAT3) in chemoresistance, cell survival, and proliferation, we investigated whether MM cells derived from patients express activated NF- κ B and STAT3 and if their suppression induces apoptosis. We assayed CD138+ cells from the

bone marrow of 22 MM patients and checked for the activated forms of NF- κ B and STAT3 by immunocytochem. We found that MM cells from all the patients expressed the activated forms of NF- κ B and STAT3 but to a variable degree (NF- κ B: low, 3 of 22; moderate, 5 of 22; or high, 14 of 22; STAT3: none, 1 of 22; low, 3 of 22; moderate, 5 of 22; or high, 14 of 22). Constitutive activation of NF- κ B was in some cases also independently confirmed by electrophoretic mobility gel shift assay. In contrast to MM patients, activated forms of NF- κ B and STAT3 were absent in cells from healthy individuals. Suppression of NF- κ B and STAT3 activation in MM cells by ex vivo treatment with **curcumin** (diferuloylmethane) resulted in a decrease in adhesion to bone marrow stromal cells, cytokine secretion, and in the viability of cells. When compared with **curcumin**, **dexamethasone** was less effective in suppression of NF- κ B activation and induction of apoptosis in myeloma cells. Overall, our results indicate that fresh cells from MM patients express constitutively active NF- κ B and STAT3, and suppression of these transcription factors inhibits the survival of the cells.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:2635 HCAPLUS

DOCUMENT NUMBER: 140:70995

TITLE: Treatment of human **multiple myeloma** with **curcumin**

INVENTOR(S): Aggarwal, Bharat

PATENT ASSIGNEE(S): Research Development Foundation, USA

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000229	A2	20031231	WO 2003-US19837	20030624
WO 2004000229	A3	20040304		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2489947	AA	20031231	CA 2003-2489947	20030624
US 2004058021	A1	20040325	US 2003-602303	20030624
EP 1523318	A2	20050420	EP 2003-761285	20030624
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-390926P	P 20020624
			WO 2003-US19837	W 20030624

AB All **multiple myeloma** cell lines examined showed constitutively active I κ B kinase (IKK), I κ B α phosphorylation and constitutively active NF- κ B. **Curcumin**, a chemopreventive agent, suppressed constitutive I κ B α

phosphorylation through inhibition of IKK activity and downregulated NF- κ B. **Curcumin** also downregulated expression of NF- κ B-regulated gene products such as I κ B α , Bcl-2, Bcl-xL, cyclin D1, and interleukin-6. Consequently, **curcumin** suppressed **multiple myeloma** cell proliferation and arrested cells at the G1/S phase of the cell cycle. **Curcumin** also induced apoptosis and chemosensitivity to **vincristine**. Overall, the results provide a mol. basis for the treatment of **multiple myeloma** patients with this pharmacol. safe agent.

L4 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2003:875065 HCAPLUS
 DOCUMENT NUMBER: 139:358741
 TITLE: Synergistic effects of nuclear transcription factor NF- κ B inhibitors and antineoplastic agents for the treatment of tumors and tumor metastases
 INVENTOR(S): Aggarwal, Bharat
 PATENT ASSIGNEE(S): Research Development Foundation, USA
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090681	A2	20031106	WO 2003-US12617	20030424
WO 2003090681	A3	20040826		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2483340	AA	20031106	CA 2003-2483340	20030424
US 2004002499	A1	20040101	US 2003-422292	20030424
EP 1496880	A2	20050119	EP 2003-718509	20030424
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-375288P	P 20020424
			WO 2003-US12617	W 20030424

AB The invention provides methods of inhibiting metastasis of a tumor and methods of treating a tumor using a combination of an inhibitor of the activation of nuclear factor NF- κ B and a cancer chemotherapeutic agent. In one embodiment of the invention, combination of **curcumin** and paclitaxel (Taxol) can be used to treat and inhibit metastasis of a breast tumor.

L4 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2003:790896 HCAPLUS
 DOCUMENT NUMBER: 139:390906
 TITLE: **Curcumin** (diferuloylmethane) inhibits constitutive and IL-6-inducible STAT3 phosphorylation

in human **multiple myeloma** cells
AUTHOR(S): Bharti, Alok C.; Donato, Nicholas; Aggarwal, Bharat B.
CORPORATE SOURCE: Cytokine Research Section, Department of
Bioimmunotherapy, Unit 143, University of Texas M. D.
Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Immunology (2003), 171(7), 3863-3871
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous reports suggest that IL-6 promotes survival and proliferation of **multiple myeloma** (MM) cells through the phosphorylation of a cell signaling protein, STAT3. Thus, agents that suppress STAT3 phosphorylation have potential for the treatment of MM. In the present report, we demonstrate that **curcumin** (diferuloylmethane), a pharmacol. safe agent in humans, inhibited IL-6-induced STAT3 phosphorylation and consequent STAT3 nuclear translocation. **Curcumin** had no effect on STAT5 phosphorylation, but inhibited the IFN- α -induced STAT1 phosphorylation. The constitutive phosphorylation of STAT3 found in certain MM cells was also abrogated by treatment with **curcumin**. **Curcumin**-induced inhibition of STAT3 phosphorylation was reversible. Compared with AG490, a well-characterized Janus kinase 2 inhibitor, **curcumin** was a more rapid (30 min vs 8 h) and more potent (10 μ M vs 100 μ M) inhibitor of STAT3 phosphorylation. In a similar manner, the dose of **curcumin** completely suppressed proliferation of MM cells; the same dose of AG490 had no effect. In contrast, a cell-permeable STAT3 inhibitor peptide that can inhibit the STAT3 phosphorylation mediated by Src blocked the constitutive phosphorylation of STAT3 and also suppressed the growth of myeloma cells. TNF- α and lymphotoxin also induced the proliferation of MM cells, but through a mechanism independent of STAT3 phosphorylation. In addition, **dexamethasone**-resistant MM cells were found to be sensitive to **curcumin**. Overall, our results demonstrated that **curcumin** was a potent inhibitor of STAT3 phosphorylation, and this plays a role in the suppression of MM proliferation.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:90410 HCAPLUS

DOCUMENT NUMBER: 139:30341

TITLE: **Curcumin** (diferuloylmethane) down-regulates the constitutive activation of nuclear factor- κ B and I κ B α kinase in human **multiple myeloma** cells, leading to suppression of proliferation and induction of apoptosis

AUTHOR(S): Bharti, Alok C.; Donato, Nicholas; Singh, Sujay; Aggarwal, Bharat B.

CORPORATE SOURCE: Cytokine Research Section, Department of Bioimmunotherapy, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Blood (2003), 101(3), 1053-1062

CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Because of the central role of the transcription factor nuclear factor- κ B (NF- κ B) in cell survival and proliferation in human **multiple myeloma** (MM), we explored the possibility of

Feb 2003

using it as a target for MM treatment by using **curcumin** (diferuloylmethane), an agent known to have very little or no toxicity in humans. We found that NF- κ B was constitutively active in all human MM cell lines examined and that **curcumin**, a chemopreventive agent, down-regulated NF- κ B in all cell lines as indicated by electrophoretic mobility gel shift assay and prevented the nuclear retention of p65 as shown by immunocytochem. All MM cell lines showed constitutively active I κ B kinase (IKK) and I κ B α phosphorylation. **Curcumin** suppressed the constitutive I κ B α phosphorylation through the inhibition of IKK activity. **Curcumin** also down-regulated the expression of NF- κ B-regulated gene products, including I κ B α , Bcl-2, Bcl-xL, cyclin D1, and interleukin-6. This led to the suppression of proliferation and arrest of cells at the G1/S phase of the cell cycle. Suppression of NF- κ B complex by IKK γ /NF- κ B essential modulator-binding domain peptide also suppressed the proliferation of MM cells. **Curcumin** also activated caspase-7 and caspase-9 and induced polyadenosine-5'-diphosphate-ribose polymerase (PARP) cleavage. **Curcumin**-induced down-regulation of NF- κ B, a factor that has been implicated in chemoresistance, also induced chemosensitivity to **vincristine** and **melfhalan**. Overall, our results indicate that **curcumin** down-regulates NF- κ B in human MM cells, leading to the suppression of proliferation and induction of apoptosis, thus providing the mol. basis for the treatment of MM patients with this pharmacol. safe agent.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d que stat 16

L1 7 SEA FILE=REGISTRY ABB=ON (VINCRISTINE OR BCNU OR MELPHALAN OR CYCLOPHOSPHAMIDE OR ADRIAMYCIN OR PREDNISONE OR DEXAMETHASONE)/CN

L2 1 SEA FILE=REGISTRY ABB=ON CURCUMIN/CN

L3 83 SEA FILE=HCAPLUS ABB=ON (L1 OR VINCRISTINE OR BCNU OR MELPHALAN OR CYCLOPHOSPHAMIDE OR ADRIAMYCIN OR PREDNISONE OR DEXAMETHASONE) AND (L2 OR ?CURCUMIN?)

L4 7 SEA FILE=HCAPLUS ABB=ON L3 AND ?MULTIPLE?(W)?MYELOMA?

L5 14 SEA L4

L6 8 DUP REMOV L5 (6 DUPLICATES REMOVED)

=> d ibib abs 16 1-8

L6 ANSWER 1 OF 8 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004203663 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15070700

TITLE: Nuclear factor-kappaB and STAT3 are constitutively active in CD138+ cells derived from **multiple myeloma** patients, and suppression of these transcription factors leads to apoptosis.

AUTHOR: Bharti Alok C; Shishodia Shishir; Reuben James M; Weber Donna; Alexanian Raymond; Raj-Vadhan Saroj; Estrov Zeev; Talpaz Moshe; Aggarwal Bharat B

CORPORATE SOURCE: Department of Bioimmunotherapy, The University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.

SOURCE: Blood, (2004 Apr 15) 103 (8) 3175-84. Electronic Publication: 2003-12-18. Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200405

ENTRY DATE: Entered STN: 20040423
Last Updated on STN: 20040528
Entered Medline: 20040527

AB Chemoresistance is a major problem in the treatment of patients with **multiple myeloma** (MM). Because of the central role of the nuclear transcription factors nuclear factor-kappaB (NF-kappaB) and signal transducer and activator of transcription 3 (STAT3) in chemoresistance, cell survival, and proliferation, we investigated whether MM cells derived from patients express activated NF-kappaB and STAT3 and if their suppression induces apoptosis. We assayed CD138+ cells from the bone marrow of 22 MM patients and checked for the activated forms of NF-kappaB and STAT3 by immunocytochemistry. We found that MM cells from all the patients expressed the activated forms of NF-kappaB and STAT3 but to a variable degree (NF-kappaB: low, 3 of 22; moderate, 5 of 22; or high, 14 of 22; STAT3: none, 1 of 22; low, 3 of 22; moderate, 5 of 22; or high, 14 of 22). Constitutive activation of NF-kappaB was in some cases also independently confirmed by electrophoretic mobility gel shift assay. In contrast to MM patients, activated forms of NF-kappaB and STAT3 were absent in cells from healthy individuals. Suppression of NF-kappaB and STAT3 activation in MM cells by ex vivo treatment with **curcumin** (diferuloylmethane) resulted in a decrease in adhesion to bone marrow stromal cells, cytokine secretion, and in the viability of cells. When compared with **curcumin**, **dexamethasone** was less effective in suppression of NF-kappaB activation and induction of apoptosis in myeloma cells. Overall, our results indicate that fresh

cells from MM patients express constitutively active NF-kappaB and STAT3, and suppression of these transcription factors inhibits the survival of the cells.

L6 ANSWER 2 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2004455097 EMBASE
TITLE: Apoptosis of **multiple myeloma**.
AUTHOR: Oancea M.; Mani A.; Hussein M.A.; Almasan A.
CORPORATE SOURCE: Dr. A. Almasan, Depts. Cancer Biol. Radiat. Oncol., NB40,
Cleveland Clinic Foundation, Cleveland, OH 44195, United
States. almasaa@ccf.org
SOURCE: International Journal of Hematology, (2004) Vol. 80, No. 3,
pp. 224-231.
Refs: 76
ISSN: 0925-5710 CODEN: IJHEEY
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041112
Last Updated on STN: 20041112

AB **Multiple myeloma** (MM) is a malignancy of terminally differentiated plasma cells. MM cells localize to the bone marrow, where cell adhesion-mediated autocrine or paracrine activation of various cytokines, such as interleukin 6, insulin-like growth factor 1, and interferon α , results in their accumulation mainly because of loss of critical apoptotic controls. Resistance to apoptosis, a genetically regulated cell death process, may play a critical role in both pathogenesis and resistance to treatment of MM. Abnormalities in regulation and execution of apoptosis can contribute to tumor initiation, progression, as well as to tumor resistance to various therapeutic agents. Apoptosis is executed via 2 main pathways that lead to activation of caspases: the death receptor (extrinsic) pathway and the mitochondrial (intrinsic) pathway. Ionizing radiation and chemotherapeutic agents act primarily through the intrinsic pathway, in which mitochondria play the central role. Various therapeutic modalities that are effective in MM modulate levels of the proapoptotic and antiapoptotic Bcl-2 family of proteins and of inhibitors of apoptosis, expression of which is primarily regulated by p53, nuclear factor κ B, and STAT (signal transducers and activators of transcription) factors. This review focuses on the key concepts and some of the most recent studies of signaling pathways regulated in MM and summarizes what is known about the clinical role of these pathways. .COPYRGT. 2004 The Japanese Society of Hematology.

L6 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003441010 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14500688
TITLE: **Curcumin** (diferuloylmethane) inhibits
constitutive and IL-6-inducible STAT3 phosphorylation in
human **multiple myeloma** cells.
AUTHOR: Bharti Alok C; Donato Nicholas; Aggarwal Bharat B
CORPORATE SOURCE: Cytokine Research Section, Department of Bioimmunotherapy,
Unit 143, University of Texas M. D. Anderson Cancer Center,

AB Numerous reports suggest that IL-6 promotes survival and proliferation of **multiple myeloma** (MM) cells through the phosphorylation of a cell signaling protein, STAT3. Thus, agents that suppress STAT3 phosphorylation have potential for the treatment of MM. In the present report, we demonstrate that **curcumin** (diferuloylmethane), a pharmacologically safe agent in humans, inhibited IL-6-induced STAT3 phosphorylation and consequent STAT3 nuclear translocation. **Curcumin** had no effect on STAT5 phosphorylation, but inhibited the IFN-alpha-induced STAT1 phosphorylation. The constitutive phosphorylation of STAT3 found in certain MM cells was also abrogated by treatment with **curcumin**. **Curcumin**-induced inhibition of STAT3 phosphorylation was reversible. Compared with AG490, a well-characterized Janus kinase 2 inhibitor, **curcumin** was a more rapid (30 min vs 8 h) and more potent (10 micro M vs 100 micro M) inhibitor of STAT3 phosphorylation. In a similar manner, the dose of **curcumin** completely suppressed proliferation of MM cells; the same dose of AG490 had no effect. In contrast, a cell-permeable STAT3 inhibitor peptide that can inhibit the STAT3 phosphorylation mediated by Src blocked the constitutive phosphorylation of STAT3 and also suppressed the growth of myeloma cells. TNF-alpha and lymphotoxin also induced the proliferation of MM cells, but through a mechanism independent of STAT3 phosphorylation. In addition, **dexamethasone**-resistant MM cells were found to be sensitive to **curcumin**. Overall, our results demonstrated that **curcumin** was a potent inhibitor of STAT3 phosphorylation, and this plays a role in the suppression of MM proliferation.

Searched by Mary Jane Ruhl Ext. 22524 Page 20

ENTRY DATE: Entered STN: 20030117
Last Updated on STN: 20030422
Entered Medline: 20030421

AB Because of the central role of the transcription factor nuclear factor-kappaB (NF-kappaB) in cell survival and proliferation in human **multiple myeloma** (MM), we explored the possibility of using it as a target for MM treatment by using **curcumin** (diferuloylmethane), an agent known to have very little or no toxicity in humans. We found that NF-kappaB was constitutively active in all human MM cell lines examined and that **curcumin**, a chemopreventive agent, down-regulated NF-kappaB in all cell lines as indicated by electrophoretic mobility gel shift assay and prevented the nuclear retention of p65 as shown by immunocytochemistry. All MM cell lines showed constitutively active IkappaB kinase (IKK) and IkappaBalpha phosphorylation. **Curcumin** suppressed the constitutive IkappaBalpha phosphorylation through the inhibition of IKK activity. **Curcumin** also down-regulated the expression of NF-kappaB-regulated gene products, including IkappaBalpha, Bcl-2, Bcl-x(L), cyclin D1, and interleukin-6. This led to the suppression of proliferation and arrest of cells at the G(1)/S phase of the cell cycle. Suppression of NF-kappaB complex by IKKgamma/NF-kappaB essential modulator-binding domain peptide also suppressed the proliferation of MM cells. **Curcumin** also activated caspase-7 and caspase-9 and induced polyadenosine-5'-diphosphate-ribose polymerase (PARP) cleavage. **Curcumin**-induced down-regulation of NF-kappaB, a factor that has been implicated in chemoresistance, also induced chemosensitivity to **vincristine** and **melphalan**. Overall, our results indicate that **curcumin** down-regulates NF-kappaB in human MM cells, leading to the suppression of proliferation and induction of apoptosis, thus providing the molecular basis for the treatment of MM patients with this pharmacologically safe agent.

L6 ANSWER 5 OF 8 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2004054433 EMBASE
TITLE: Nuclear factor-κB as a predictor of treatment response in breast cancer.
AUTHOR: Garg A.K.; Hortobagyi G.N.; Aggarwal B.B.; Sahin A.A.; Buchholz T.A.
CORPORATE SOURCE: Dr. T.A. Buchholz, Department of Radiation Oncology, Univ. TX M. D. Anderson Cancer Ctr., Unit 97, 1515 Holcolmbe Blvd., Houston, TX 77030, United States.
tbuchhol@mdanderson.org
SOURCE: Current Opinion in Oncology, (2003) Vol. 15, No. 6, pp. 405-411.
Refs: 111
ISSN: 1040-8746 CODEN: CUOOE8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 014 Radiology
016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040304
Last Updated on STN: 20040304

AB Purpose of review: To examine the links of nuclear factor-κB (NF-κB) to treatment-induced signaling in breast cancer and to

propose further studies to elucidate the role of NF- κ B in breast cancer response to chemotherapy and radiation. Recent findings: The authors' group and others have investigated the clinical relevance of ubiquitously expressed NF- κ B in breast cancer. Possibly through its effects on apoptosis, NF- κ B has been implicated in tumor resistance to chemotherapy and radiation in many types of tumors. Furthermore, both in vitro and in vivo studies have shown that targeted inhibition of NF- κ B can sensitize tumor cells to chemotherapy and radiation. Summary: The molecular mechanisms involved in chemotherapy-induced and radiation-induced cell death in breast cancer are not fully known, nor are the mechanisms of treatment resistance. NF- κ B is a transcription factor for a number of genes involved in tumor progression and resistance to systemic therapies and is a major regulator of the apoptotic pathway. Gaining further insights into molecular factors such as NF- κ B as biomarkers for treatment response may help clinicians predict treatment outcome and lead to the development of targeted therapeutics.

L6 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
 ACCESSION NUMBER: 2004:184577 BIOSIS
 DOCUMENT NUMBER: PREV200400181675
 TITLE: Differential effects of the combination of **curcumin** with conventional chemotherapeutic agents on human **multiple myeloma** cells.
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AB **Curcumin**, a polyphenol found in the spice turmeric, is the major yellow pigment used in curries. **Curcumin** was shown to induce apoptosis in cancer cells and was thought to have a chemopreventive effect. Inactivation of NF-kappaB, inhibition of c-Jun N-terminal kinase, downregulation of cell surface adhesion molecules, cyclin D1, bcl-2 and MMP-9, inhibition of protein kinase C and activation of caspases were the most common effects due to **curcumin** in tumor cell lines. The aim of this study was to evaluate, whether the addition of **curcumin** to widely used cytostatic drugs in the treatment of **multiple myeloma**, e.g. **melphalan**, doxorubicin and **dexamethasone**, could enhance or inhibit the induction of apoptosis and could inhibit growth in human **multiple myeloma** cells. Using the MTT-assay, we found that **curcumin** inhibits the growth of freshly isolated human bone marrow myeloma cells and myeloma cell lines in a dose dependent manner (10-100 μ M). The addition of **curcumin** to 1 μ M **melphalan** could slightly increase the apoptosis in all examined cell lines. When **curcumin** was added to doxorubicin (100, 250 or 1000 nM), we

observed a reduced growth inhibition in U266 and LP-1 cells in comparison to doxorubicin alone, and an enhanced growth inhibition in RPMI-S. In all examined cell lines, the addition of 10 μ M **curcumin** to 1 or 5 μ M **dexamethasone** failed to enhance apoptosis. Interestingly, in freshly isolated myeloma cells from bone marrow aspirates from patients. 100 and 250 nM doxorubicin reduced the pro-apoptotic effect of **curcumin**. In conclusion, our data show that **curcumin** inhibits myeloma cell growth and induces apoptosis when applied alone. The addition of **curcumin** to **melphalan** increased the pro-apoptotic effect of **curcumin**, but **curcumin** antagonized doxorubicin and **dexamethasone**. The inhibition of doxorubicin-induced apoptosis may be related to the inhibition of reactive oxygen species and c-Jun N-terminal kinase by **curcumin**. Addition of **curcumin** to other chemotherapeutic agents should occur with caution.

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AB Given its role in cellular metabolism, the proteasome could prove to be a critical target that can be exploited in treating cancer. In preclinical studies, several mechanisms for bortezomib's activity in **multiple myeloma** cells have been identified (e.g., NF- κ B inhibition); antitumor activity with bortezomib has been seen in myeloma patients, thereby supporting the validity of the preclinical work. Similar mechanisms may be in play in solid tumors, and cell culture and xenograft data suggest bortezomib may be active in a wide range of tumor types. One promising possibility is the use of bortezomib for the treatment of chemoresistant tumors. Chemoresistance can be caused by a number of cellular factors; NF- κ B is a prominent instigator of chemoresistance, and proteasome inhibition was an effective means of preventing NF- κ B activation in myeloma and several solid tumor laboratory studies. However, the inhibition of NF- κ B may not be the only mechanism for antitumor activity. This review explores the use of proteasome inhibitors to subvert intrinsic resistance mechanisms, disrupt inducible chemoresistance, or augment the mechanisms of action of standard chemotherapeutics. Thus, in addition to providing another target for anticancer treatment, proteasome inhibition may also provide a means to treat refractory tumors. .COPYRG. 2003 Elsevier Science Ltd. All rights reserved.

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